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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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DUNSTON, JENNIFER ANN	
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1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,112	MORI ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *46-54,57,58 and 60-63* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *46-54,57,58 and 60-63* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *01 July 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 8/30/2011, in which claims 24, 31, 37, 39, 40, 56 and 64 were cancelled, claims 46-48, 50-54 and 57 were amended. Claims 46-54, 57, 58 and 60-63 are pending and under consideration.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Claim Objections

Claim 46 is objected to because of the following informalities:

The phrase "into the RNA virus vector cDNA" is redundant and unnecessary. Lines 12-13 recite "cDNA of a RNA virus vector having incorporated therein." It would be remedial to delete the phrase "into the RNA virus vector cDNA."

Appropriate correction is required.

Response to Arguments - Claim Objections

The previous objection of claim 46 has been withdrawn in view of the amendment to the claim in the reply filed 8/30/2011.

Response to Arguments - 35 USC § 112

The rejection of claim 57 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment to the claim in the reply filed 8/30/2011.

The rejection of claim 64 under 35 U.S.C. 112, second paragraph, is moot in view of Applicant's cancellation of the claim in the reply filed 8/30/2011.

The rejection of claim 57 under 35 U.S.C. 112, fourth paragraph, has been withdrawn in view of Applicant's amendment to the claim in the reply filed 8/30/2011.

The rejection of claim 64 under 35 U.S.C. 112, fourth paragraph, is moot in view of Applicant's cancellation of the claim in the reply filed 8/30/2011.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 46-48, 50, 51, 57, 58 and 60-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mori et al (The Plant Journal, Vol. 27, No. 1, pages 79-86, 2001, cited on the

IDS filed 3/31/2006; see the entire reference) in view of David et al (Plant Physiology, Vol. 125, pages 1548-1553, April 2001, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 5/31/2011 and has been rewritten as necessitated by the amendments to the claims in the reply filed 8/30/2011.

Mori et al teach a process for producing a transformant for protein production, comprising (i) transforming *N. benthamiana* host cells with plasmid pTA7001BB1 comprising a GVG transcription factor-expressing DNA fragment in which the GVG coding sequence is operably linked to the CaMV 35S promoter, and the 6xUASgal4 promoter is linked to the 1a gene; where transforming is done by an Agrobacterium method (ii) screening the transformants obtained in step (i) for an individual F0 plant expressing GVG; and (iii) crossing the F0 GVG-expressing plants with 2FR plants containing plasmid pBICHGCP2IFNR comprising cDNA of a RNA virus vector that has been constructed by inserting a coding gene of human gamma interferon (IFN) into an RNA virus, where a ribozyme sequence of satellite tobacco ringspot virus is ligated to the 3' end of the RNA virus vector cDNA (e.g., page 82, *Production of transgenic plants containing cDNA of RNA1 or cDNAs of both RNA2 and FCP2IFN*; pages 82-83, *Induced replication of FCP2IFN and subgenomic mRNA amplification in GVG1 x 2FR plants*; page 85, *Transformation of Nicotiana benthamiana*; Figure 1). Specifically, plasmid pBICHGCP2IFNR used in the method of Mori et al contains a cDNA of a Brome mosaic virus having incorporated therein a coding sequence of a human gamma interferon (IFN) protein, and ligating a ribozyme sequence to the 3' end of the Brome mosaic virus (RNA virus) vector cDNA (e.g., page 85, paragraph bridging columns; Figure 1). The ribozyme sequence is a ribozyme sequence of satellite tobacco ringspot virus (e.g., page 85, paragraph bridging columns). In the

virus vector, the IFN sequence was inserted in place of the coat protein gene (e.g., page 80, right column, 2nd full paragraph). Further, Mori et al teach a transformant produced by the abovementioned process, where the transformant produces IFN protein in the presence of dexamethasone (e.g., Figure 4). Mori et al teach that the GVG transcription factor has a property of being activated by the hormone dexamethasone, a synthetic steroid hormone (e.g., page 82, *Analysis of the accumulation of RNA1 in response to DEX treatment*). Mori et al teach the method where the virus vector originates in a virus that is a Brome mosaic virus, which is a single strand (+) RNA plant virus (e.g., page 80, right column, 2nd full paragraph).

Mori et al do not teach the method where the GVG transformants are further transformed with the cDNA of a virus vector that encodes IFN using an Agrobacterium method. Further, Mori et al do not teach the method where the cells are tobacco BY-2 cells.

David et al teach that the tobacco (*Nicotiana tabacum*) BY2 cell line is well characterized, highly homogenous, and shows an exceptionally high growth rate (e.g., page 1548, left column, 1st paragraph). Further, David et al teach that BY2 cells can be easily transformed without the need for protoplast preparation and stable transgenic calli, and suspension-cultured cells are easily obtained (e.g., page 1548, left column, 1st paragraph). David et al teach a method that brings together the advantages of the BY2 cell line with the advantages of the tetracycline derepressible system (e.g., page 1548, right column, full paragraph). David et al teach a method for producing a transformant for protein production, comprising (i) transforming BY2 cells with pBinTet1 vector, containing tetR under the control of the cauliflower mosaic virus (CaMV)-35S promoter; (ii) selecting clonal and stable transformants, named BY2-tetR, on kanamycin medium; (iii) and transforming the BY2-tetR cells with a pTX-

Gus-int, a vector containing β-glucuronidase (Gus) under the control of the "Triple-Op" promoter coupled with CaMV 35S (e.g., paragraph bridging pages 1548-1549; page 1549, left column). David et al teach that Gus activity was induced in the BY2-tetR cells comprising pTX-Gus-int by the addition of AhTc (e.g., Figure 1). David et al teach that a high steady-state expression of tetR ensures an efficient repression of the "Triple-Op" promoter (e.g., paragraph bridging pages 1549-1550). David et al teach Agrobacterium-mediated transformation of the BY2 cells (e.g., page 1552, Cell Transformation).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Mori et al to include a first Agrobacterium-mediated transformation step of BY2 cells with the GVG expression vector, and a second Agrobacterium-mediated transformation step of BY2 cells with the IFN expression vector, as taught by David et al because David et al teach it is within the ordinary skill in the art to use BY2 cells for regulated expression of a protein product and Mori et al teach regulated expression of the IFN protein product.

One would have been motivated to make such a modification in order to receive the expected benefit of selecting for BY2 GVG transformants with desirable levels of GVG expression prior to transformation with the IFN expression vector, because David et al teach that desirable levels of tetR could be identified prior to the second transformation step. It would have been within the ordinary skill of the art to transform the BY2 cells based upon the teachings of David et al, and it would have been within the skill of the art to screen for desirable levels of GVG by Northern blotting as taught by Mori et al. Furthermore, one would have been motivated to perform a second transformation step in BY2 cells rather than produce plants and cross the

plants as taught by Mori et al in order to save time, because David et al teach that BY2 cells have an exceptionally high growth rate and are easy to transform. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mori et al (The Plant Journal, Vol. 27, No. 1, pages 79-86, 2001, cited on the IDS filed 3/31/2006; see the entire reference) in view of David et al (Plant Physiology, Vol. 125, pages 1548-1553, April 2001, cited in a prior action; see the entire reference) as applied to claims 46-48, 50, 51, 57, 58 and 60-63 above, and further in view of Zuo et al (US Patent No. 6,452,068 B1, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 5/31/2011 and is reiterated below. The rejection statement has been rewritten to remove reference to the cancelled claims.

The combined teachings of Mori et al and David et al are described above and applied as before.

Mori et al and David et al do not teach the method where the transcription factor is LexA-VP16-hER, the inducible promoter is O_{LexA}-46, and the inducer is estrogen.

Zuo et al teach the vector where the transcription factor is a chimeric transcription factor in which the regulatory region lf the rat GR is added to the DNA-binding domain of the yeast transcription factor GAL4 and the transactivating domain of the herpes viral protein VP16, where the chimeric transcription factor is called GVG (e.g., column 9, lines 50-67). When the

vector comprises the GVG transcription factor, the inducible promoter contains six copies of the GAL4 upstream activating sequence (UAS) (6xUASGal4, e.g., column 9, lines 50-67; Figure 1). Zuo et al teach another construct referred to as XVE, which is similar to the GVG system but contains the DNA binding domain of the bacterial repressor LexA and the regulatory region of the human estrogen receptor (e.g., column 10, lines 43-53). Zuo et al specifically teach that the XVE construct can be used in place of the GVG construct as long as the proper inducer is used for the construct being used (e.g., column 10, lines 48-51). When the vector comprises the XVE transcription factor, the inducible promoter contains eight copies of LexA binding sites fused to the 35S minimal promoter at -46 (O_{LexA}-46), and the inducer is estrogen (e.g., Example 12; Figure 13).

Mori et al and David et al both teach the use of regulatable transcription factors capable of being modulated for regulated expression of a protein. Mori et al specifically teaches the use of the GVG system, and Zuo et al specifically teaches that it was within the skill of the art to substitute the XVE system for the GVG system in order to achieve the predictable result of providing inducible expression of a protein. The XVE system comprises the claimed LexA-VP16-hER transcription factor, which is activated by estrogen, and the O_{LexA}-46 promoter.

Claims 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mori et al (The Plant Journal, Vol. 27, No. 1, pages 79-86, 2001, cited on the IDS filed 3/31/2006; see the entire reference) in view of David et al (Plant Physiology, Vol. 125, pages 1548-1553, April 2001, cited in a prior action; see the entire reference) as applied to claims 46-48, 50, 51, 57, 58 and 60-63 above, and further in view of Rasochova et al (US Patent Application Publication No.

2003/0074677 A1, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 5/31/2011 and is reiterated below. The rejection statement has been rewritten to remove reference to the cancelled claims.

The combined teachings of Mori et al and David et al are described above and applied as before.

Mori et al and David et al do not teach the method where the virus vector comprises tobacco mosaic virus.

Rasochova et al teach a vector comprising cDNA of an RNA virus vector that has been constructed by inserting an exogenous RNA component and a ribozyme sequence at the 3' region (e.g., paragraph [0049]). Rasochova et al teach the vector where the exogenous RNA component has a coding function in which the RNA acts as a messenger RNA, encoding a sequence which, when translated by the host cell, results in the synthesis of a peptide or protein (e.g., paragraph [0047]). Rasochova et al teach the vector where the virus vector originates in a virus that is a single strand (+) RNA virus, such as tobacco mosaic virus (e.g., paragraphs [0042], [0135], [0139] and [0141]). Rasochova et al teach the DNA molecule where the exogenous RNA component is inserted in place of the coat protein coding sequence (e.g., paragraphs [0057] and [0137]). Rasochova et al teach the use of the vector to make transgenic plants expressing the protein (e.g., paragraphs [0138]-[0141]). Further, Rasochova et al teach it is within the skill of the art to use an inducible promoter for the expression of the exogenous RNA component (e.g., paragraphs [0049]-[0050]).

Because Mori et al and Rasochova et al both teach vectors for the expression of a protein in plant cells, it would have been obvious to one of ordinary skill in the art at the time the

invention was made to substitute the tobacco mosaic virus vector of Rasochova et al for the Brome mosaic virus vector of Mori et al, where expression of the protein is under the control of the 6xUASgal4 promoter, in order to achieve the predictable result of providing a vector for the inducible expression of a protein in a plant cell.

Response to Arguments - 35 USC § 103

The rejection of claims 24, 31, 37, 39 and 40 under 35 U.S.C. 103(a) as being unpatentable over Garger et al in view of Weber et al and Zuo et al is moot in view of Applicant's cancellation of the claims in the reply filed 8/30/2011.

The rejection of claims 56 and 64 under 35 U.S.C. 103(a) as being unpatentable over Mori et al in view of David et al is moot in view of Applicant's cancellation of the claims in the reply filed 8/30/2011.

With respect to the rejection of claims 46-48, 50, 51, 57, 58 and 60-63 under 35 U.S.C. 103(a) as being unpatentable over Mori et al in view of David et al, Applicant's arguments filed 8/30/2011 have been fully considered but they are not persuasive.

The response asserts that the Examiner does not address why one would be motivated to modify the alleged combination of references to include a second transformation step using a plasmid containing a RNA virus vector cDNA, because neither Mori nor David mention RNA virus vector cDNA and there is no rationale presented for modifying the alleged combination to include this feature. The response asserts that Mori does not teach expression of a viral vector cDNA. The response asserts that the Office provides no explanation of how an additional transforming step with a virus vector (not disclosed in David) may be implemented in the

process of Mori. The response asserts that the references do not teach RNA virus vector cDNA, and a ribozyme sequence ligated to the 3' end of the RNA virus vector cDNA.

These arguments are not persuasive. Mori teaches using an Agrobacterium transfection method to transfect plant cells with plasmid pBICHGCP2IFNR (e.g., page 85, *Transformation of Nicotiana benthamiana*). The plasmid used by Mori, pBICHGCP2IFNR, contains a cDNA of the Brome mosaic, where the coat protein 2 (CP2) gene was replaced by the interferon (IFN) gene coding sequence, and where the ribozyme sequence from satellite RNA of Tobacco ringspot virus was inserted at the 3' end of the cDNA of the virus RNA (e.g., page 85, *Plasmids*). Mori teaches expression of RNA from the viral vector cDNA contained within the plasmid (e.g., Fig. 1). Mori teaches that the Brome mosaic virus is a tripartite RNA virus (e.g., Abstract). This is also shown schematically in Fig. 1. Fig. 1 also shows the transcription of the BMV RNA3 derivative FCP2IFN from the 35S promoter. Fig. 1 shows the linkage of the ribozyme sequence to the 3' end of the modified BMV RNA3. Only the promoter of the plasmid is altered by the combination of Mori and David, and it would have been within the skill of the art to replace one promoter with another promoter in order to achieve the expected result of providing an expressible sequence. Furthermore, one would have been motived to use the promoter of David in order to provide regulated expression of RNA from the construct, as taught by David. Such a modification would bring together the advantages of inducible expression and the ease of use of BY-2 cells, as taught by David.

The response points to the remarks filed 9/27/2010. The response asserts that one would have expected a second transforming step to reduce expression efficiency.

These arguments are not found persuasive for the reasons set forth in the *Response to Arguments* section of the Office action mailed 5/31/2011. Furthermore, arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). Applicant has not provided evidence that one would have expected a second transformation step to reduce expression efficiency of the virus vector of Mori.

The response asserts that there would have been no reasonable expectation of success, because (1) viral vector cDNA is difficult and unpredictable, (2) viral growth at the growing point is difficult in plant culture cells vs. plants, (3) no conventional protoplast formation needed with claimed features, and (4) viral vector cDNA expression is low in plant culture cells.

The argument that viral vector cDNA being difficult and unpredictable is not found persuasive. Example 2 presents the methods and results used in the experiment of Figure 7. In Example 2, the vectors used are plasmid vectors based on the Ti plasmid pTA7001, and the vectors contain the coding sequence for GVG, the 6XUASgal4 promoter, and the ToMV variant downstream of the 6XUASgal4 promoter (e.g., page 62). BY2 cells were transformed with a plasmid control vector (sold diamond, no ribozyme sequence), a plasmid vector comprising the ribozyme sequence of hepatitis delta virus (sold squares), and a plasmid vector comprising the ribozyme sequence of satellite tobacco ringspot virus (solid circles). The phrase "PRECULTURE PERIOD (IN DAYS)" means the number of days the cells were subcultured prior to steroid hormone treatment (paragraph bridging pages 64-65). At pages 64-65, the

specification describes the following conclusions based upon the results of the experiment shown in Figure 7:

> As in clear from Figure 7, with the control vector, the percentage of GFP-expressing cells was below 5% even on day 7. On the contrary, the percentage of GFP-expressing cells was about 25% in the vector containing the ribozyme sequence of hepatitis delta virus, and about 60% in the vector containing the ribozyme sequence of satellite tobacco ringspot virus.

Accordingly, the results of the experiment demonstrate that the ribozyme sequence of satellite tobacco ringspot virus provides higher levels of expression in BY2 cells when the ribozyme is covalently bound to the 3' end of a tomato mosaic virus cDNA. These results are not commensurate in scope with the claimed invention. Furthermore, one would have been motivated to use two transformation steps in order to select cells that express high levels of the transcription factor as taught by David.

The argument that viral growth being difficult in plant culture cells vs. plants is not found persuasive. David teaches that the tobacco (*Nicotiana tabacum*) BY2 cell line is well characterized, highly homogenous, and shows an exceptionally high growth rate (e.g., page 1548, left column, 1st paragraph). Further, David teaches that BY2 cells can be easily transformed without the need for protoplast preparation and stable transgenic calli, and suspension-cultured cells are easily obtained (e.g., page 1548, left column, 1st paragraph). Applicant's argument that it is difficult to cause viral growths in all plant culture cells is not found persuasive, because the claims do not require growth in all plant culture cells. Furthermore, the plasmid taught by Mori comprises a hygromycin resistance gene as a selectable marker (e.g., page 85, *Plasmids*), and David teaches the selection of stable transformants using plasmids that contain a hygromycin resistance gene (e.g., page 1550, left column, 1st full

paragraph). Cells containing the plasmid are selected on hygromycin medium (e.g., David, page 1550, paragraph bridging columns). One of skill in the art would have understood that such a selection step would allow for removal of the cells that do not contain the plasmid comprising the cDNA of the RNA virus. Thus, one of skill in the art would have known how to avoid the problems described by Applicant at pages 11-12 of the reply.

The argument that no conventional protoplast formation needed with claimed features is not found persuasive. David teaches that the tobacco (*Nicotiana tabacum*) BY2 cell line is well characterized, highly homogenous, and shows an exceptionally high growth rate (e.g., page 1548, left column, 1st paragraph). Further, David teaches that BY2 cells can be easily transformed without the need for protoplast preparation and stable transgenic calli, and suspension-cultured cells are easily obtained (e.g., page 1548, left column, 1st paragraph). The assertion that the claims are drawn to protein expression in plant culture cells "without the formation of protoplasts" is not found persuasive. Such a limitation is not present in the rejected claims. Even if the limitation were present in the claims, David does not teach the formation of protoplasts.

The argument that viral vector cDNA expression is low in plant culture cells is not found persuasive. The assertion that only a portion of the cells will express the viral vector cDNA and that expression will be lost is not found persuasive for the reasons discussed above. Specifically, David teaches the selection of stable transformants containing the plasmid comprising the cDNA of the virus vector. Thus, the cell culture does not contain virus vectors or cells that are "chimerical" as asserted by Applicant. Furthermore, Applicant's arguments of unexpected success are not persuasive, because they are not commensurate in scope with the claimed

invention. As discussed above and in the prior action, Example 2 demonstrates that the ribozyme sequence of satellite tobacco ringspot virus provides higher levels of expression in BY2 cells when the ribozyme is covalently bound to the 3' end of a tomato mosaic virus cDNA. The claims are not limited to a tomato mosaic virus cDNA, and Mori teaches covalent linkage of a satellite tobacco ringspot virus to the 3' end of the Brome mosaic virus RNA virus vector cDNA. The obviousness rejection is not based upon the addition of the ribozyme, because the ribozyme sequence is already present in the plasmid of Mori. Furthermore, Example 3 of the specification is insufficient to overcome the rejection for the reasons set forth in the prior action.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

With respect to the rejection of claim 49 under 35 U.S.C. 103(a) as being unpatentable over Mori et al in view of David et al, and further in view of Zuo et al, Applicant's arguments filed 8/30/2011 have been fully considered but they are not persuasive.

The response asserts that the Examiner has failed to show how David and Zuo remedy the deficiencies of Mori with respect to independent claim 46. Thus, the response asserts that claim 49 is patentable over Mori, David and Zuo for the reasons set forth above with respect to independent claim 46.

This argument is not found persuasive for the reasons set forth above with regard to the rejection of claim 46.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Claims 52-54 under 35 U.S.C. 103(a) as being unpatentable over Mori et al in view of David et al, and further in view of Rasochova et al, Applicant's arguments filed 8/30/2011 have been fully considered but they are not persuasive.

The response asserts that the Examiner has failed to show how David and Rasochova remedy the deficiencies of Mori with respect to independent claim 46.

This argument is not found persuasive for the reasons set forth above.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is (571)272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Dunston/
Primary Examiner
Art Unit 1636